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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,226	08/19/2003	Ashley I. Bush	0609.4810002	3164

26111 7590 05/09/2006

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 05/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,226	BUSH ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-17 and 24-38* is/are pending in the application.

4a) Of the above claim(s) *4-17,24-35 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 August 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

1. Claim number 38 is amended. Claims 1-3 and 18-23 are cancelled.

Election/Restrictions

2. Applicant's election without traverse of Group VII, represented by claims 36 and 37, [drawn to a method for the identification of an agent to be used in the treatment of Alzheimer's disease (AD) and/or symptoms thereof, wherein said agent is capable of inhibiting redox-reactive metal-mediating cross-linking by amyloid beta peptide (Aβ)], in the reply filed on March 14, 2006 is acknowledged.

3. Claims 36 and 37 are under consideration in the instant application. Claims 4-17, 24-35 and 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected Invention, there being no allowable generic or linking claim.

Information Disclosure Statement

4. The IDS filed on 10 June 2004 has been considered.

5. References AR 52 and AR 67 could not be located and, therefore, were not considered. Applicants are invited in response to this office action only to submit copies of those references. References so submitted will be considered as though they have been filed with the IDS of 10 June 2004. Any submission of those references after the response to this office action will not be considered to be timely.

Entries that do not comply, because they are duplicated or refer to a publication that is not present in the file, are lined through.

Specification

6. The disclosure is objected to because of the following informalities:

7a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims to be considered are directed.

The following title is suggested: "METHOD FOR THE IDENTIFICATION OF A PHARMACOLOGICAL AGENT THAT INHIBITS AMYLOID β CROSS-LINKING".

Appropriate correction is required.

7b. The following figures are objected to under 37 CFR 1.83.

i) Fig 2C: The drawing depicts turbidometric analysis of pH effect on high concentrations of metal ion induced $A\beta_{1-40}$ (amyloid beta) aggregation. Description of drawing in specification (page 12, line 16), however, describes the proportion of soluble $A\beta_{1-42}$ remaining in supernatant after incubation with high metal ion concentrations.

ii) Fig 10: Figure legends describing bars are duplicated [for example, +Zn(II)].

iii) Fig 15C: has no legend.

Appropriate correction is required.

Claim Rejections - 35 USC § 112-Second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 36 and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 36 recites the limitation "said candidate pharmacological agent" in final sentence of the claim, whereas the preamble reads “an agent”. There is insufficient antecedent basis for this limitation in the claim.

11. Amendment of the preamble to recite “a candidate pharmacological agent” instead of “an agent” would be remedial.

12. It is noted that amendment of the claim to indicate that the agent can be used in treatment as opposed to being a “candidate agent” would be found not to be enabled under 35 USC § 112-first paragraph.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claim 36 is rejected under 35 U.S.C. 102(b) as clearly anticipated by Dyrks et al (Journal of Biological Chemistry 267, page 18210-18217, 1992 – cited by Applicant).

15. Claim 36 is rejected under 35 U.S.C. 102(b) because Dyrks et al teach the aggregation of amyloid beta peptide (βA4) and its precursor A4CT (amyloid precursor protein fragment comprising the complete sequence of βA4 peptide at the N-terminal position) after incubating βA4 with a redox-reactive metal ferrous chloride ($FeCl_2$) for 1 hour at 37°C (page 18214, figure 7). Dyrks et al further teach the incubation of A4CT (or βA4) with FeCl2 in the presence or absence of radical scavengers like ascorbic acid or a vitamin E derivative which result in the inhibition of protein cross-linking (page18213, figure 4 and page 18214, para 1). Furthermore, in the concluding paragraph of the reference (page 18216), Dyrks et al suggest that metal mediated reactions lead to insoluble amyloid protein aggregates involved in the pathology leading to Alzheimer's disease. Because of the similarity in the method steps disclosed by Dyrks et al and the instant application taken with Dyrks' suggestion of a link to Alzheimer's disease, the method described in the reference anticipates the invention.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claim 37 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dyrks et al (J Biol Chem 267, 18210-18217, 1992).

18. Claim 37 recites a Western blot analysis for determining the presence or absence of Aβ (amyloid beta) cross-linking. It encompasses the method of claim 36, which is a method of identification of an agent capable of inhibiting redox-reactive metal cross-linking.

19. Dyrks et al teach that insoluble aggregates of βA4 peptide are generated by metal-catalyzed cross-linking (page 18214, figure 7).

20. Dyrks et al also teach that βA4 bearing amyloid precursor fragment (A4CT) aggregates generated by metal catalyzed cross-linking are causes for amyloid plaques in AD (page 18216, last para) and that such aggregates can be analyzed by Western blot (page 18214, figure 5).

21. Dyrks et al does not teach the analysis of βA4 protein cross-linking by Western blot.

22. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to look for the presence or absence of βA4 cross-linking as disclosed by Dyrks et al (page 18214, figure 7) for the purpose of identifying βA4 peptides involved in AD, using Western blot assay with a reasonable expectation of success. One would be motivated to look for βA4 protein cross-linking, because Dyrks et al disclose that A4CT is an amyloid

precursor peptide fragment comprising the complete sequence of βA4 protein of AD at the N-terminal position (abstract-page 18210; results-page18212).

Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

23. No claims are allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

25. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

26. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see

http://pair-direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
28 April 2006

LORRAINE SPECTOR
PRIMARY EXAMINER